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Wireless Sensing

THE NEW PARADIGM

Wireless Cardiovascular Pressure Measurement Systems: Applied Nanotechnology

Jason White, Director of Biomedical Engineering, CardioMEMS Inc.

May 27, 2010

Agenda

- **Unmet Medical Needs in Pressure Sensing**
- **CardioMEMS Founded**
- **Technology Concept and Philosophy**
- **Multidisciplinary R&D Effort**
  - **MEMS: Sensor**
  - **Biomedical: Delivery Catheter and Sensor External Features**
  - **RF Engineering: External Measurement System**
- **Heart Failure Application and Pivotal Clinical Study for PMA Approval**

Pressure Monitoring: Applicable to Many Therapeutic Areas

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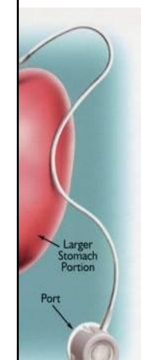
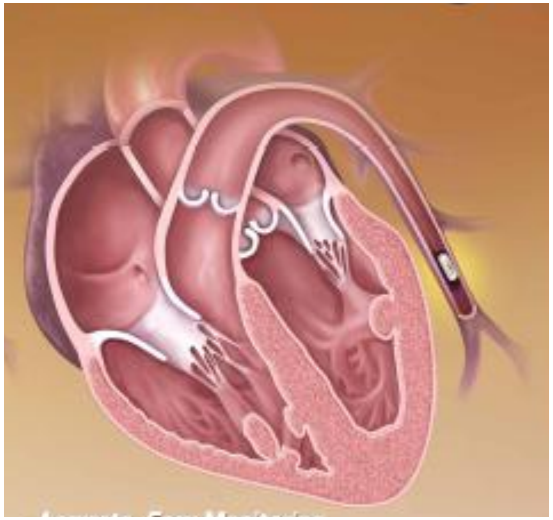
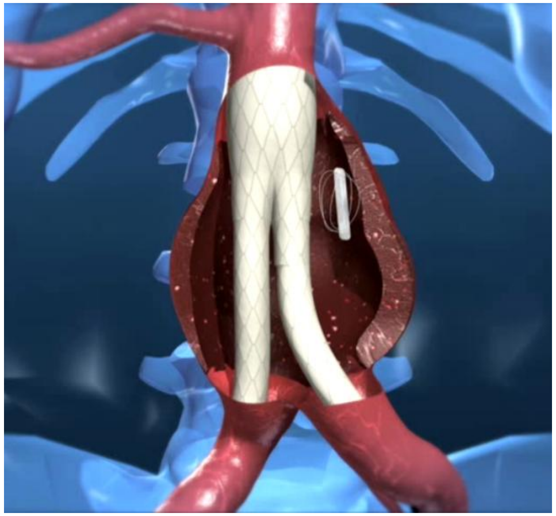


Heart Failure



Aortic Aneurysms



Orthop

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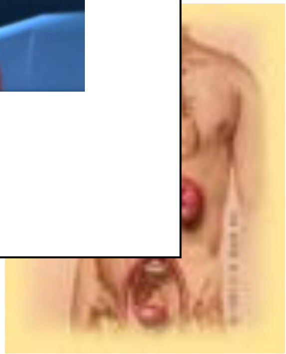

Heart Failure:
Shift from Acute to Chronic Disease Management

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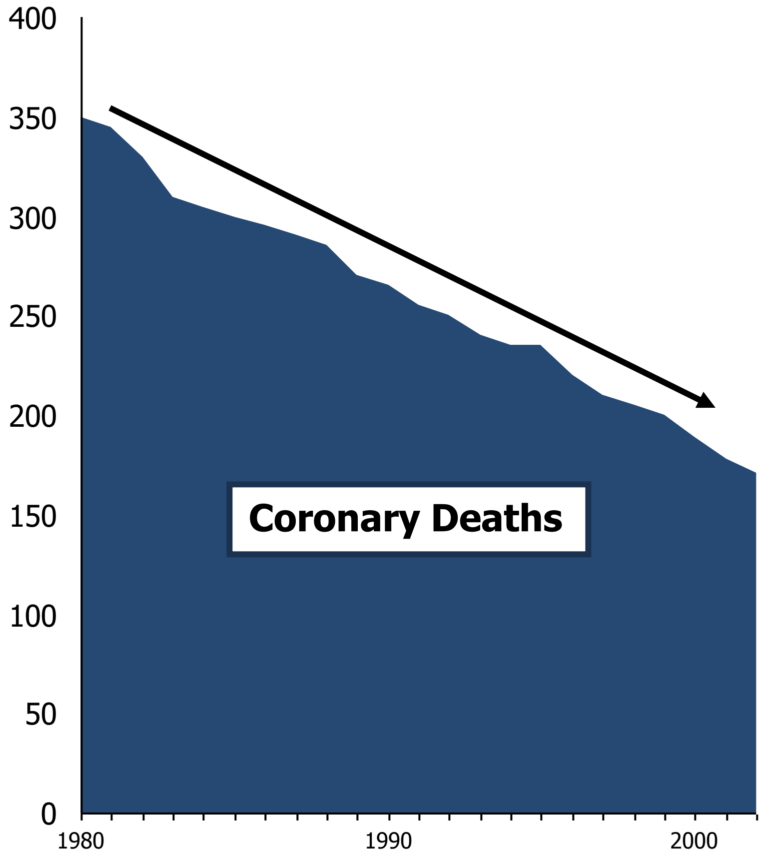
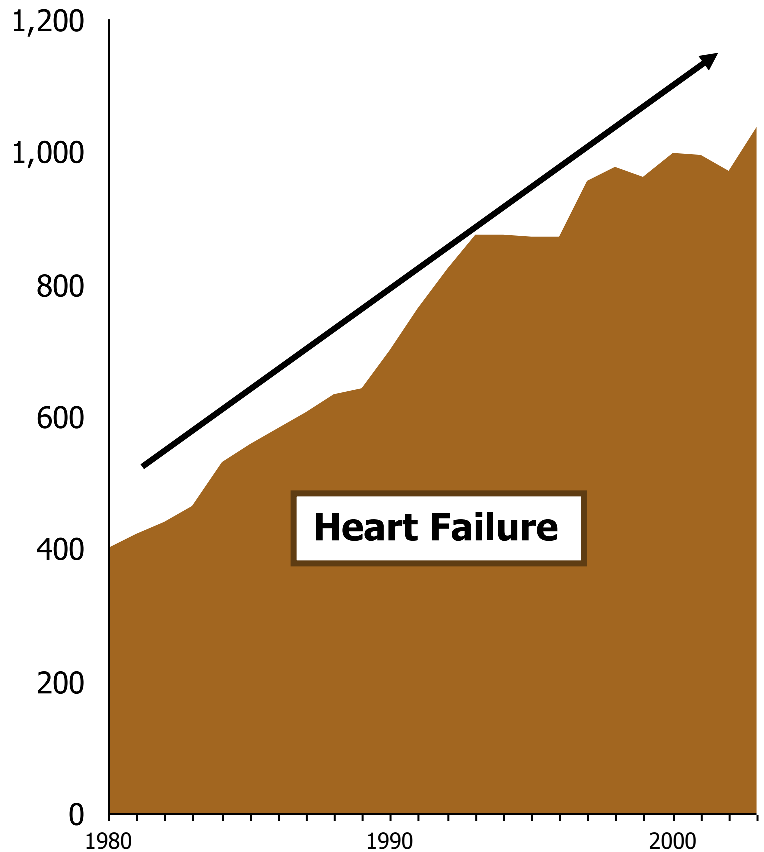
Coronary deaths are down by half…



But heart failure has almost tripled



Worse 5 year survival rate than any cancer except lung cancer

Source: National Hospital Discharge Survey, CDC/NCHS and NHLBI.

Heart Failure: Nature of Problem

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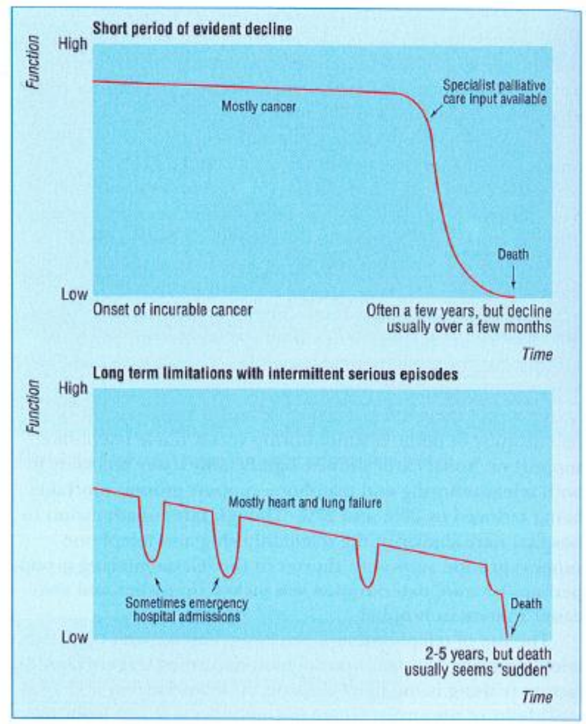
The cost of failure by Hal A. Skopicki, MD, August 2007

"What about the long-term mortality ramifications of actions taken during the acute hospitalization? Although more than 90% of heart failure patients are hospitalized with volume overload, less than 50% lose more than 5 pounds during the acute hospitalization.[8] This may reflect the difficulty in clinically assessing persistent volume overload[9] or the fear of inducing renal dysfunction in a patient population where renal function predicts not only in-hospital but also long-term mortality".[10-14]

"It is therefore surprising that no technologically pragmatic application exists to guide the aggressiveness of diuresis or to gauge when euvolemia has been established."

	Survival (%)	
Disease	1-Year	5-Year
Prostate cancer	99	99
Melanoma	98	66-92
Breast cancer	76	89
Colon cancer	82	62
Ovarian cancer	76	45
Leukemia	63	51
Heart failure	63	21
Lung cancer	42	16



Disease trajectories of terminal conditions. Heart failure tends to follow the unpredictable course shown in the lower graph. Adapted from Murray SA, et al. *BMJ* 2005;330:1007–11

How to Reduce HF Hospitalizations?

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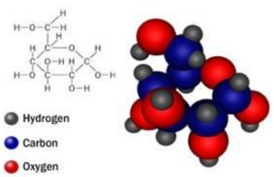
In the same way that…

Blood Glucose

Diabetes

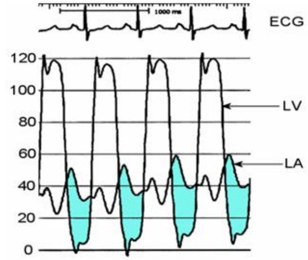


DRIVES

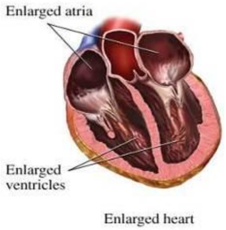
We know that…

Intracardiac Pressure

Heart Failure



DRIVES



Proactively managing cardiovascular pressure is critical to chronic management of HF

Study Design:
Monitoring Can Reduce Hospitalizations

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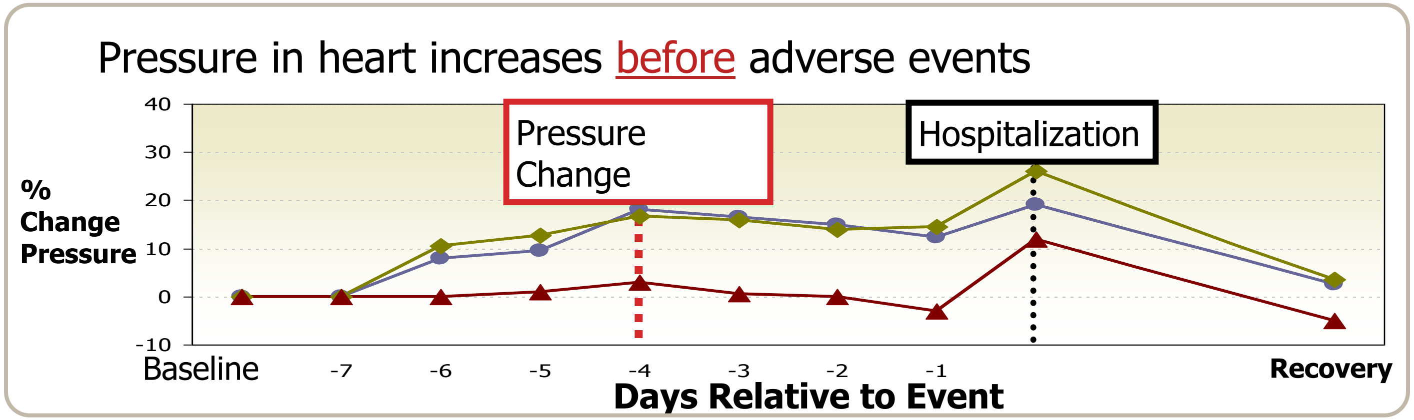


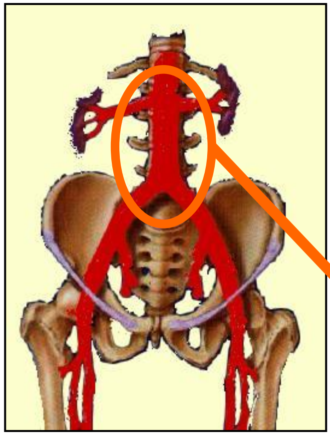
Source: Journal of the American College of Cardiology, Adamson PB et al. J Am Coll Cardiol.2003; 41: 565.

Medtronic COMPASS Trial: 274 pts, Class 3 & 4

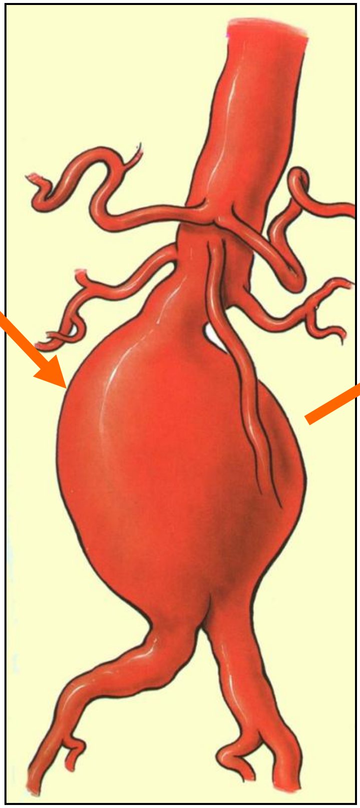
Measure	p[(a)]	% Decline
Reduction in the rate of HF events	p=0.33	↓ 21%
Reduction in the proportion of patients with worsening heart failure	p=0.035	↓ 36%
Reduction in heart failure event: Class 3 patients	p=0.03	↓ 41%

(a) p values less than 0.05 are considered statistically significant.

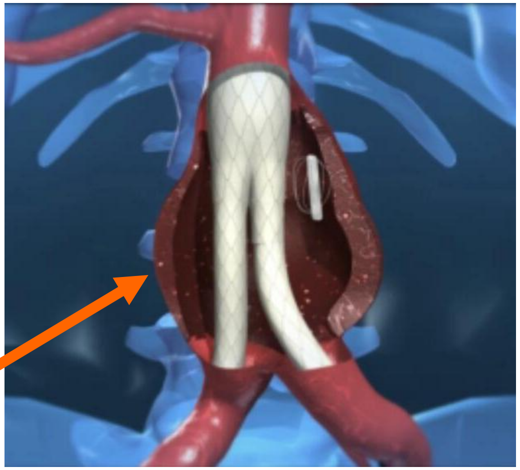
Aortic Aneurysms: Monitoring Challenge



Normal Abdominal Aorta



Diseased



Repaired by Endovascular Graft

<u>Goal of Endovascular Repair:</u>

Reduce Pressure and Wall Strain to Prevent Rupture

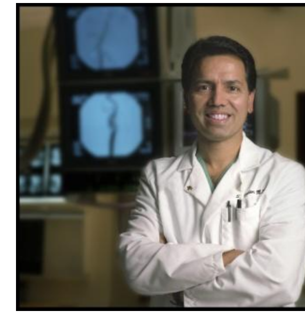
<u>Long Term Monitoring Challenge:</u>

Potential for Re-Pressurization via Leaks: Monitored by Contrast Tomography (CT)

- **Safety – radiation, contrast toxicity**
- **Accuracy**
- **Cost**
- **Inconvenience**

<u>Wireless Sensor as a Monitoring Alternative</u>

CardioMEMS Founders



Jay Yadav, M.D.

CEO and Chairman of the Board, CardioMEMS Inc

Interventional Cardiologist, Piedmont Hospital

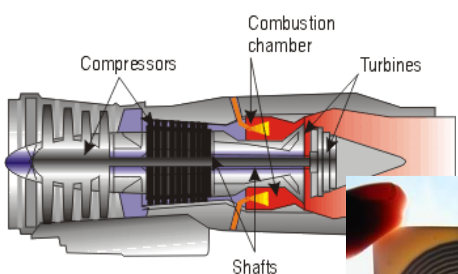
Founder and Chairman of AngioGuard, Inc. (sold to J&J in 1998)

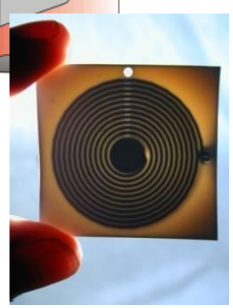
Mark Allen, Ph.D.

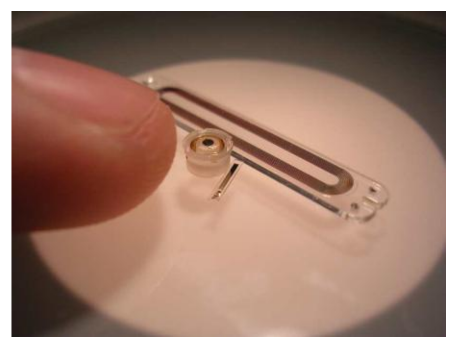
Chief Technology Officer, CardioMEMS Inc.

Senior Vice Provost for Research and Innovation; Joseph M. Pettit Professor; Regents Professor, Georgia Institute of Technology.

Co-founder, Redeon (acquired by BioValve in 2001)







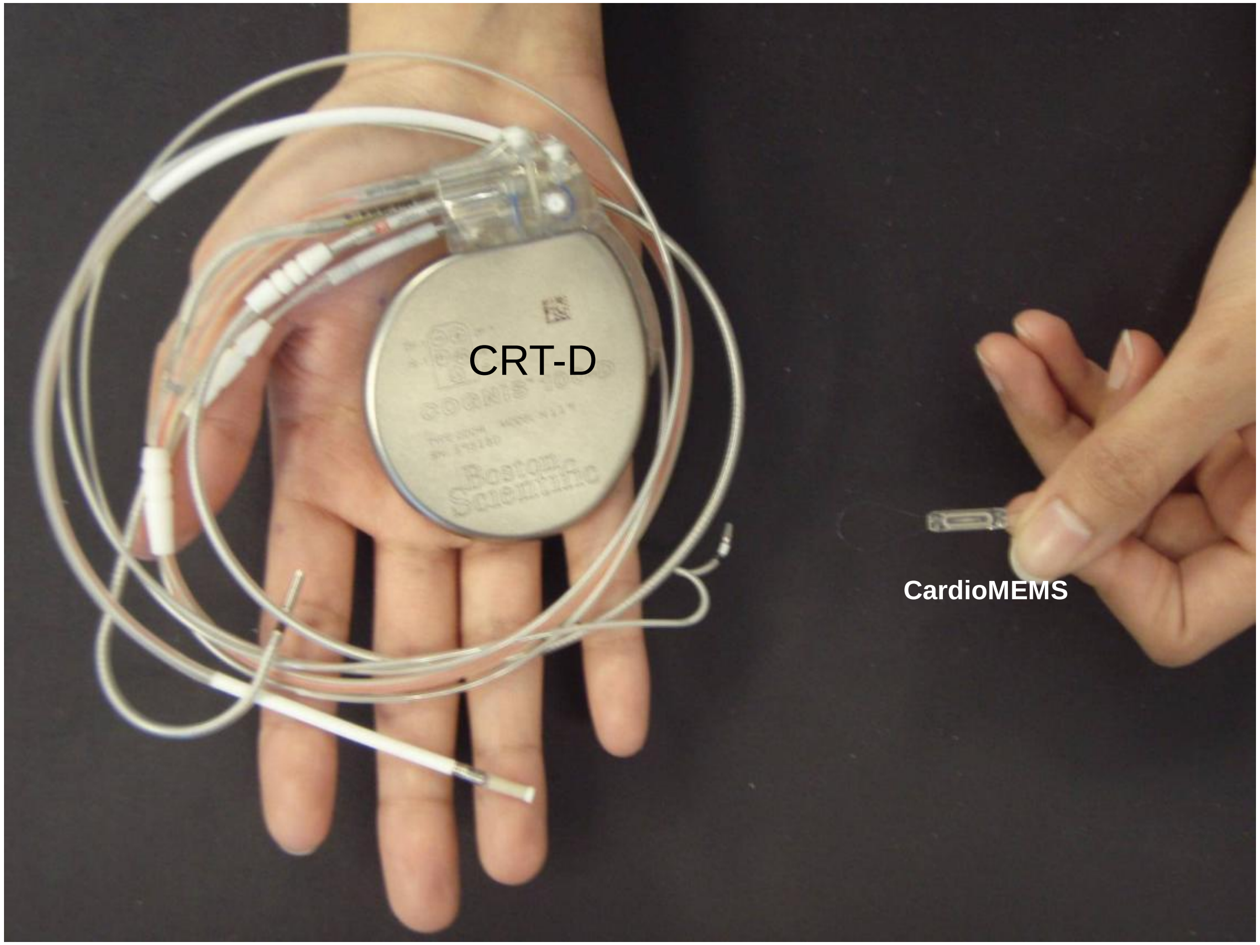
Licensed Core IP from Georgia Tech and MIT

CardioMEMS at a Glance

- Founded 2001
- Approximately 65 employees
- Aortic Aneurysm Sensor
  - FDA 510k Clearance
  - Over 7,000 sold & implanted

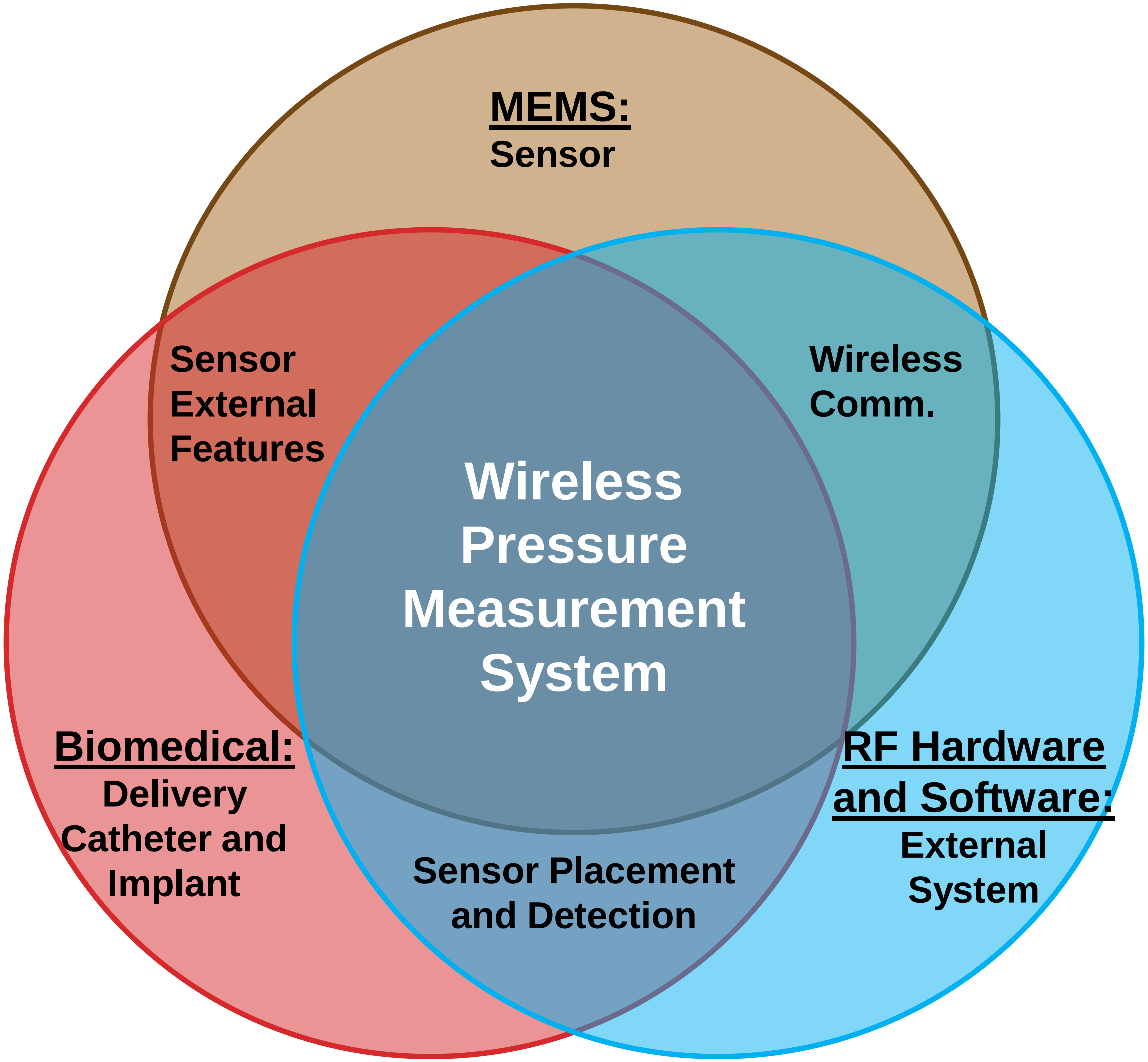
- Heart Failure Sensor
  - 550 Patient Pivotal Clinical Study Completed – Results Pending
  - > 600 implanted in clinical studies worldwide.
- Only approved, permanently implanted wireless sensor

Design Philosophy: Size and Complexity Matters



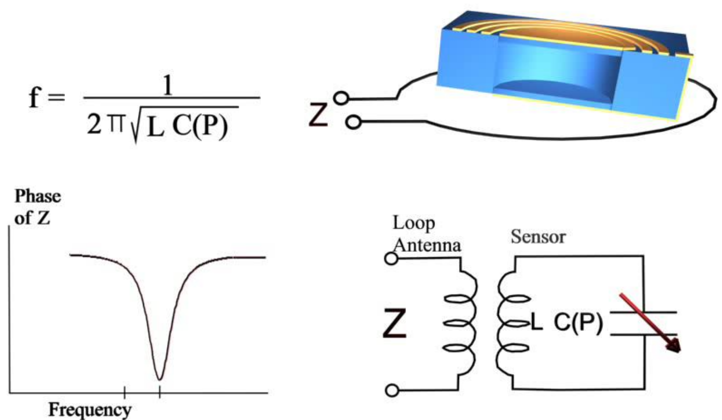
Minimize Implant Complexity and Size to Reduce Potential Failure Modes

Multidisciplinary Development Approach



Sensor Frequency to Pressure Translation

Electromagnetic Vibration of the Sensor Circuit is based on
Electrical Characteristics



Equivalent Circuit

Measurement of **Pressure**
is Based on
Frequency of Electromagnetic
Resonant Circuit

Analogous Concept:
Mechanical Vibration of a Tuning Fork is Based on
Mechanical Characteristics

$$f = \frac{R}{\pi l^2}\sqrt{\frac{E}{\rho}}$$

Passive Wireless Pressure: Appealing Concept

Implantable Sensor for Physiological Parameter Measurement

76 April, 1967 IEEE TRANSACTIONS ON BIO-MEDICAL ENGINEERING, APRIL 1967

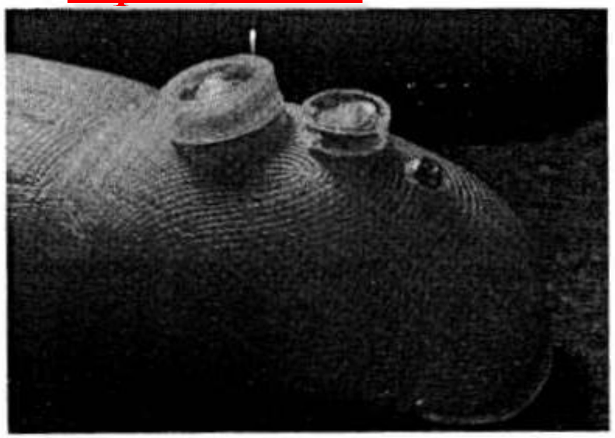
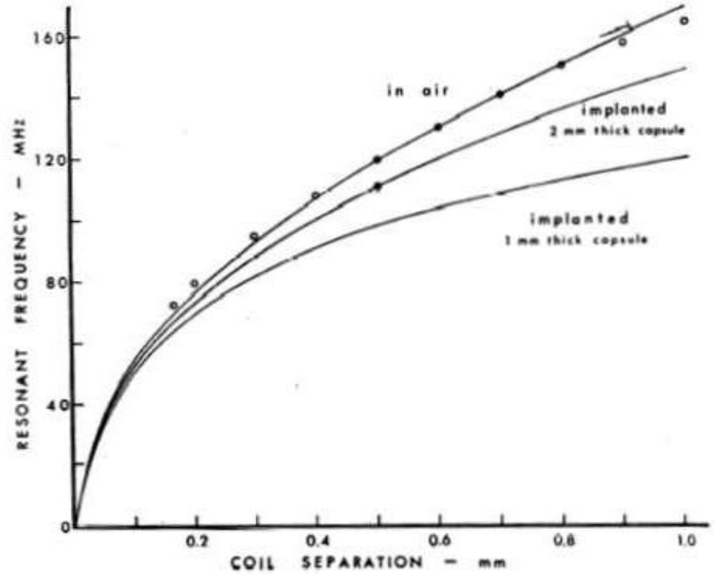


Fig. 3. Bubble tonometers 6, 4, and 2 mm in diameter. The smallest tonometer displayed here was detected when implanted in the anterior chamber of the eye, but requires further development. The larger models are used when pressures are desired from progressively deeper structures.



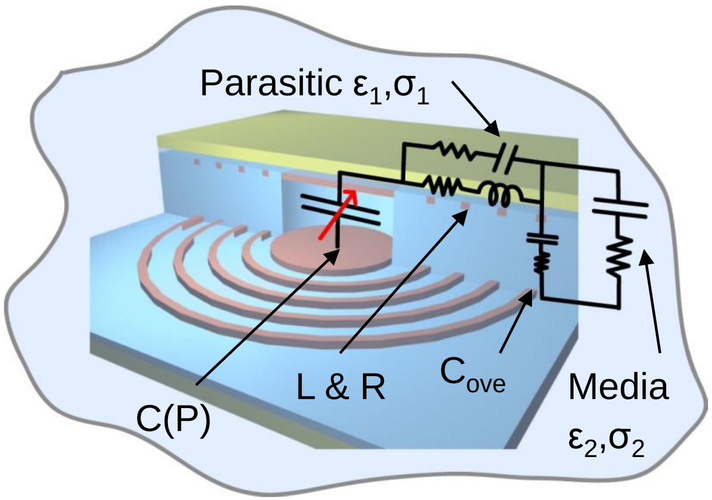
C. Collins, IEEE Trans. Biomedical Engineering

<u>Further Learning and Innovation Required:</u>

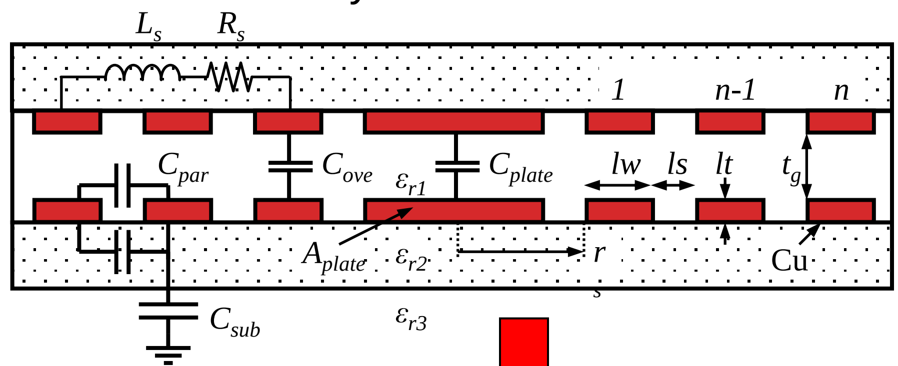
- **Long Term Stability** – Material and Process Selection
- **Detection Distance** – RF Innovation and Chipset Advancements
- **Miniaturization for Minimally Invasive Implant** – MEMS
- **Scalable Manufacturing Method** – MEMS

Research: Fundamental Understanding

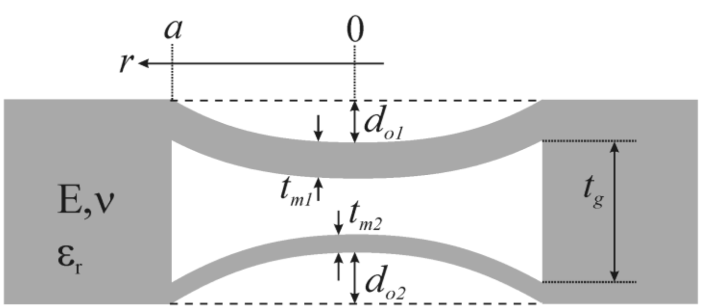
Electromagnetic Model

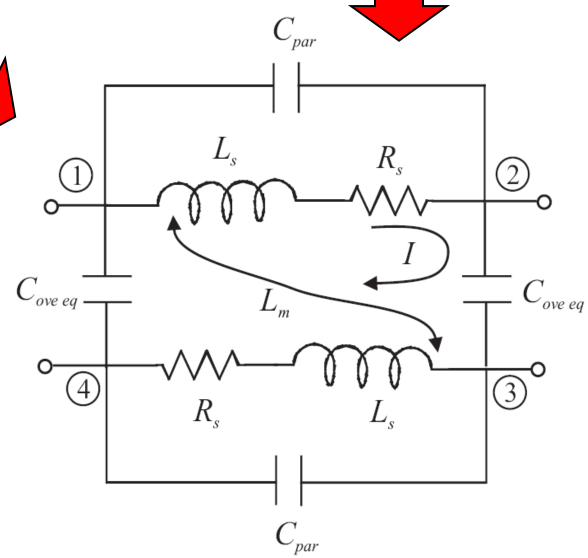


Analytical definition



Mechanical Model



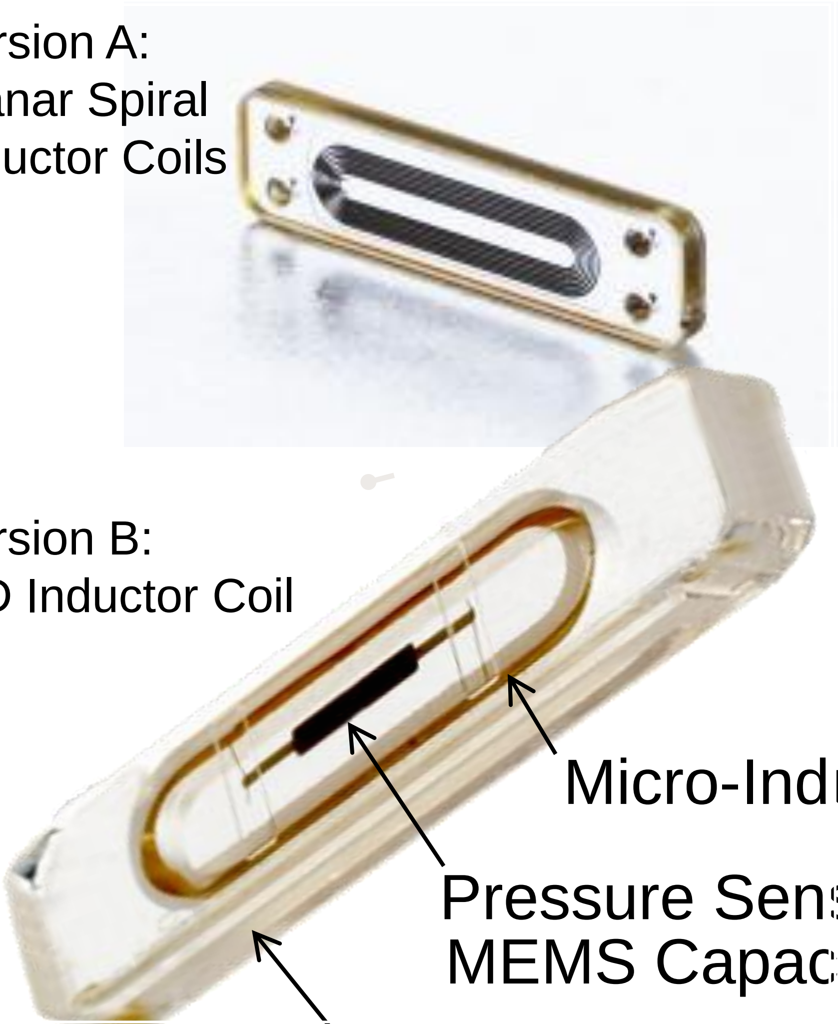


Model Verification

Sensor Attributes and Features

Version A:
Planar Spiral
Inductor Coils

Version B:
3-D Inductor Coil



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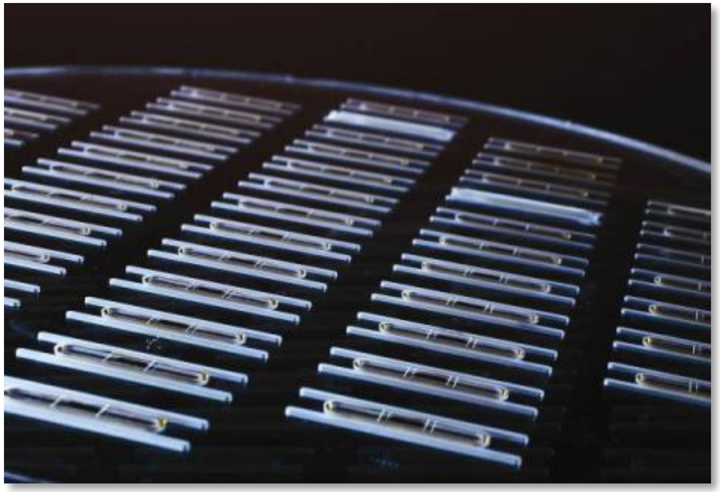
Multiple sensors fabricated in a wafer batch

Nano Scale Sensor Features

Pressure Sensitive MEMS Capacitor:

Design:
~ 1 µm Capacitor Air Gap
~ 1 nm Deflection / mm Hg



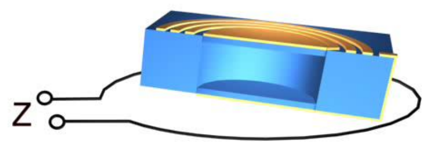
Across 6" Wafer:
+/- 12nm Electrode Height Uniformity
+/- 100nm Trench Depth

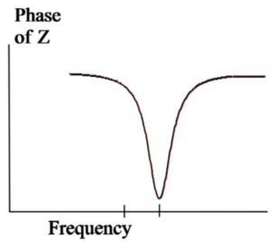
Materials:
Dimensional Stability for Baseline within +/-2 mmHg/year = +/- ~2nm/year

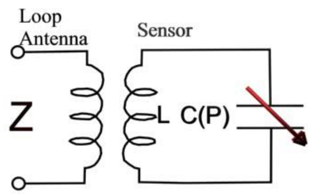
Sensor Frequency to Pressure Translation

Electromagnetic Vibration of the Sensor Circuit is based on
Electrical Characteristics

$$f = \frac{1}{2\pi\sqrt{L\,C(P)}}$$







Equivalent Circuit

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Frequency of Electromagnetic
Resonant Circuit

Analogous Concept:
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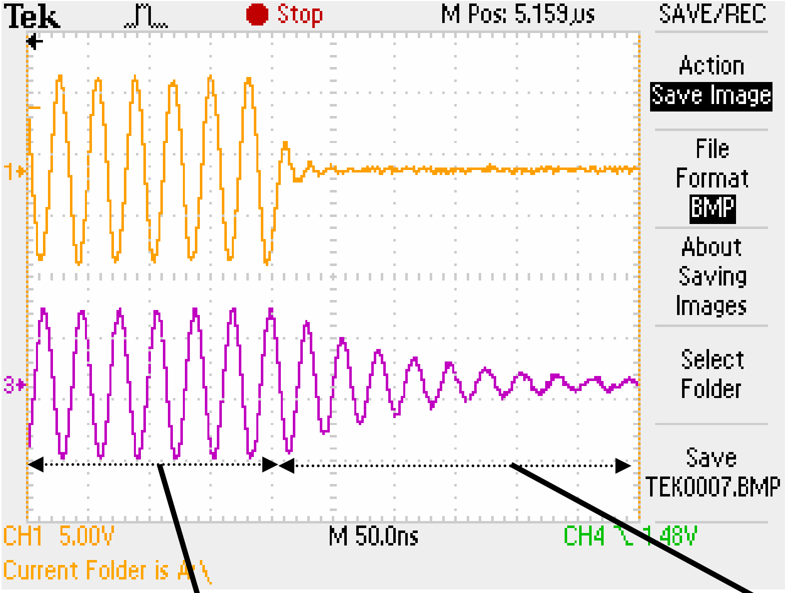
$$f = \frac{R}{\pi l^2}\sqrt{\frac{E}{\rho}}$$

External Measurement System: Communication

External Electronics

Implanted Sensor



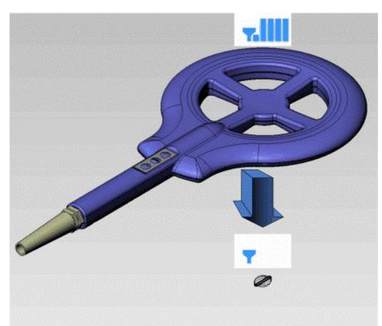
A 2us burst of RF is sent to the sensor via magnetic “loosely coupled transformer” coupling.

During the excitation burst, the sensor reacts at the same frequency as it gathers energy.

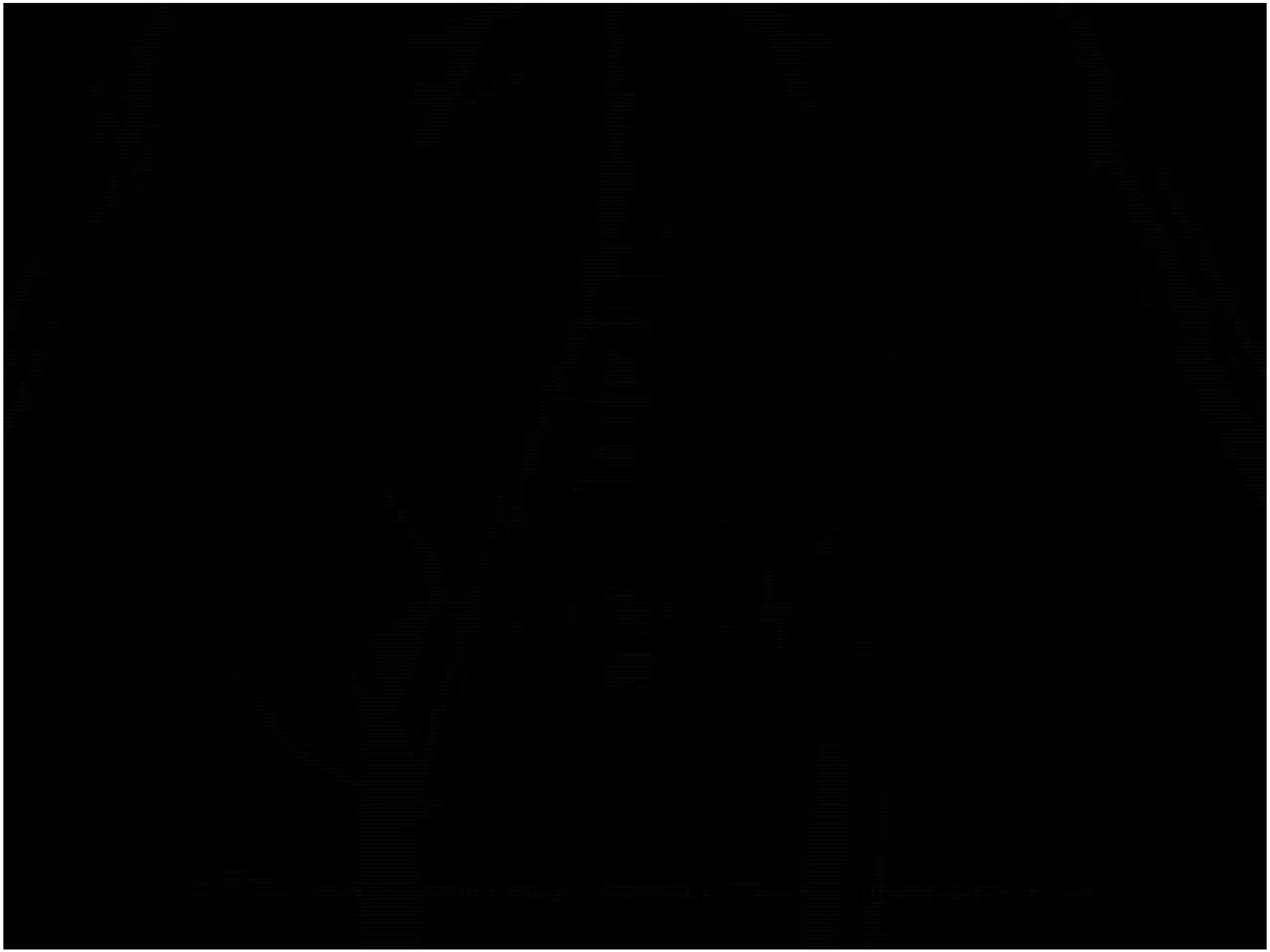
When the excitation is removed, the sensor “free-wheels” at its natural resonant frequency, which is a function of PRESSURE.

Theory of Operation

- Sensor signal decays completely within 2 μs
- Transmit / Receive Power
  - Transmit: ~0.9 W
  - Receive: ~100pW (1 billionth of a Watt)
- Sensor signal sample must be collected within 35 ns of transmit burst, due to rapid decay.
- Sampling rate: 100kHz



Heart Failure Implant and Use Animation



Introduction: Pulmonary Artery Anatomy

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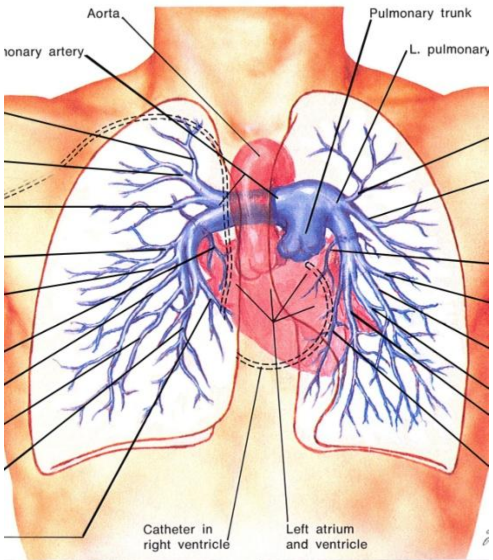
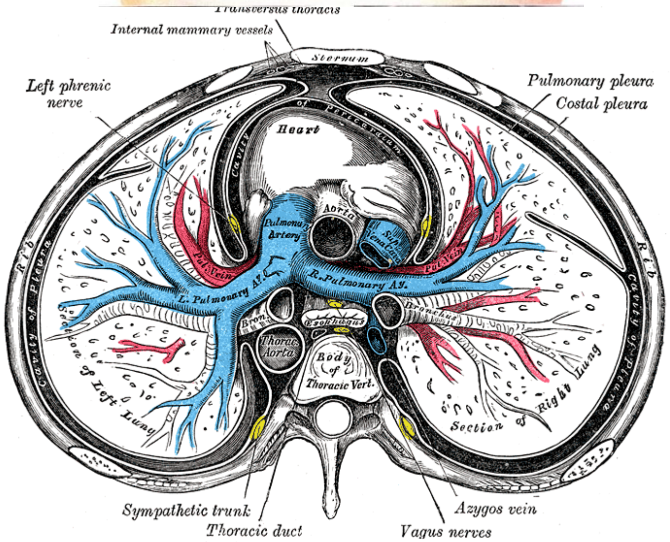
R



L



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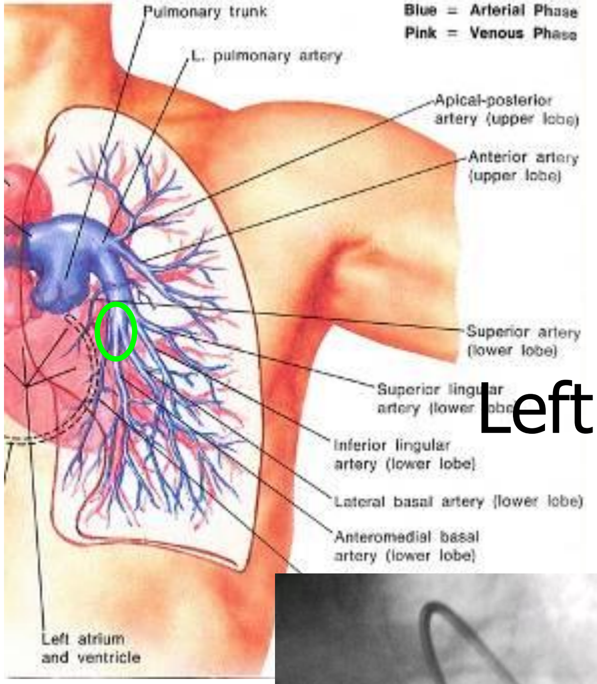
Pulmonary Artery Implant Site:

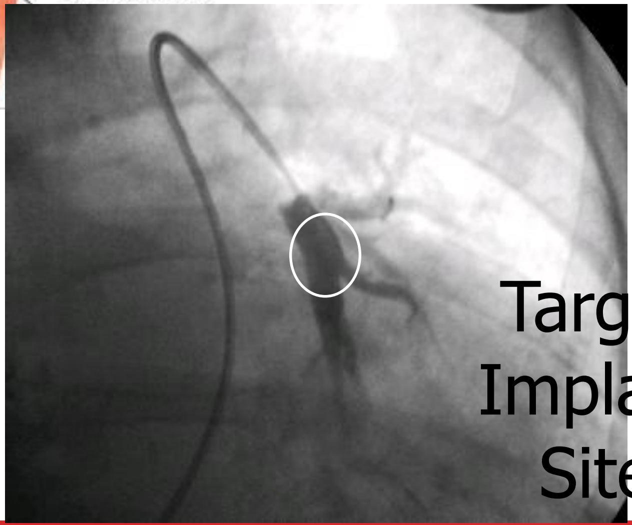
- PA pressure – key parameter of cardiac function.
- PA placement – lower risk profile than alternate implant sites.
  - Right side – no stroke risk
  - No active fixation required
- PA placement – simple implant procedure.

Target Implant Site Characteristics

- Right or left PA branch, basal (lower) lobe, descending branch, pre-bifurcation
- Within 4" of side and back
- Vessel Lumen ID approx. 7-15mm
- Aligned with long axis of body



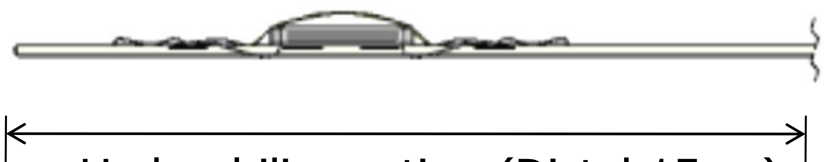
Left PA, Lower Lobe



Target Implant Site

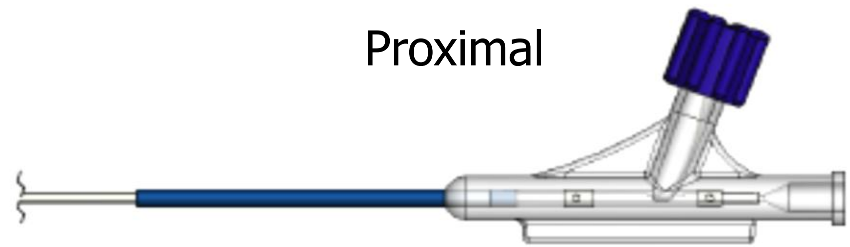
HF Delivery System

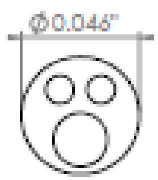
Distal



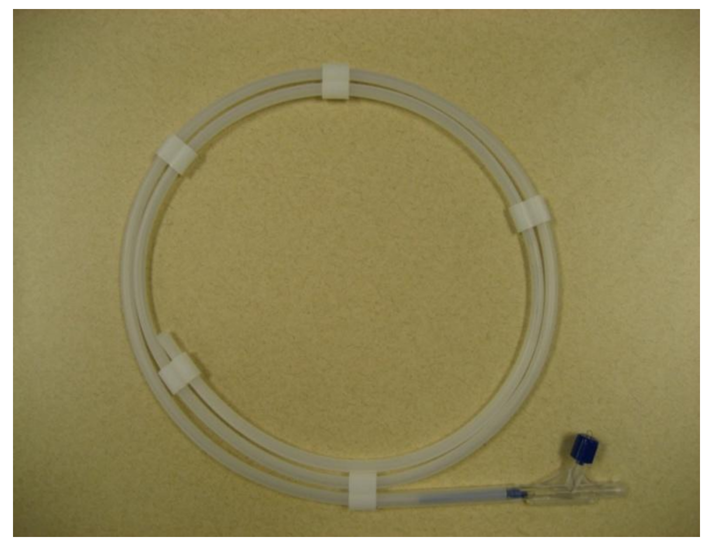
Hydrophilic coating (Distal 15cm)

Proximal

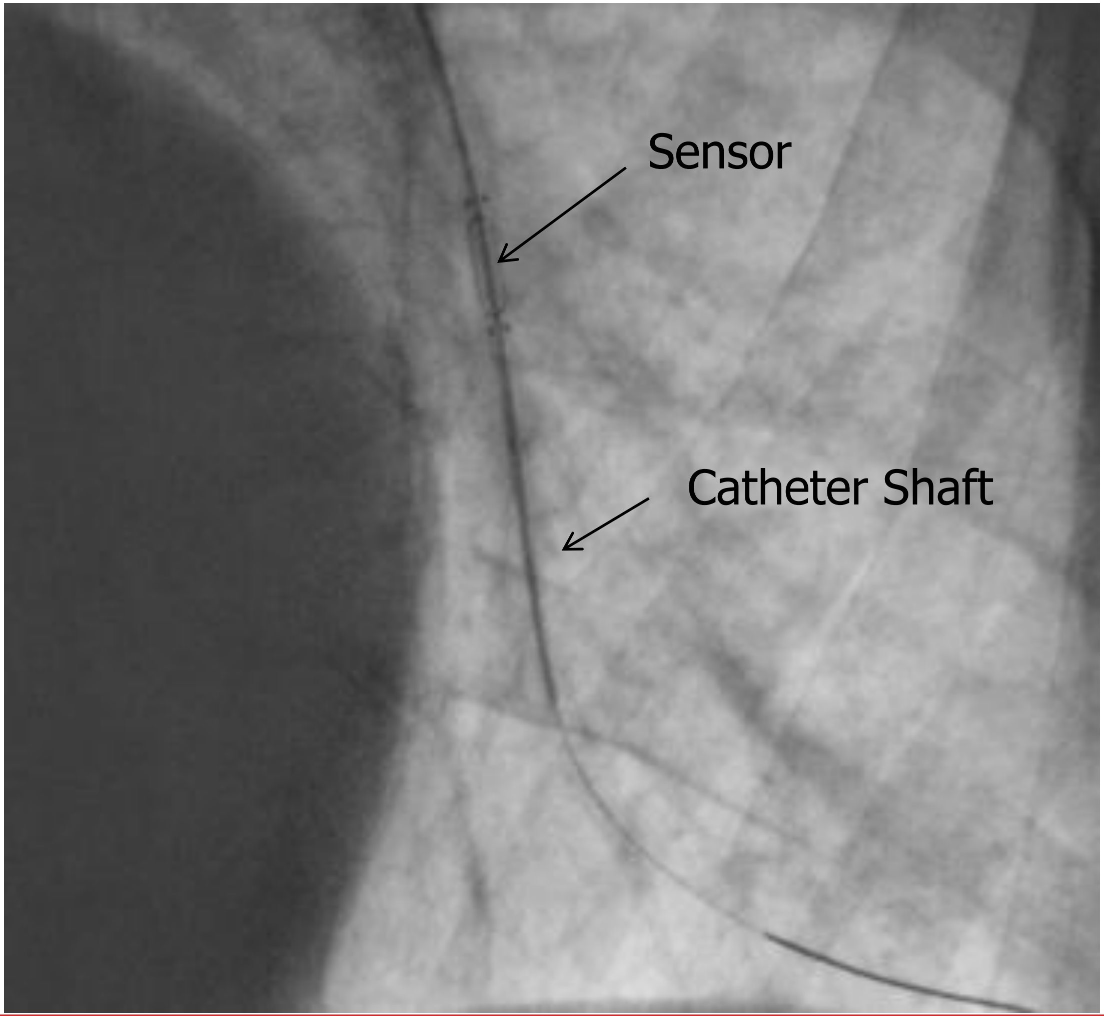




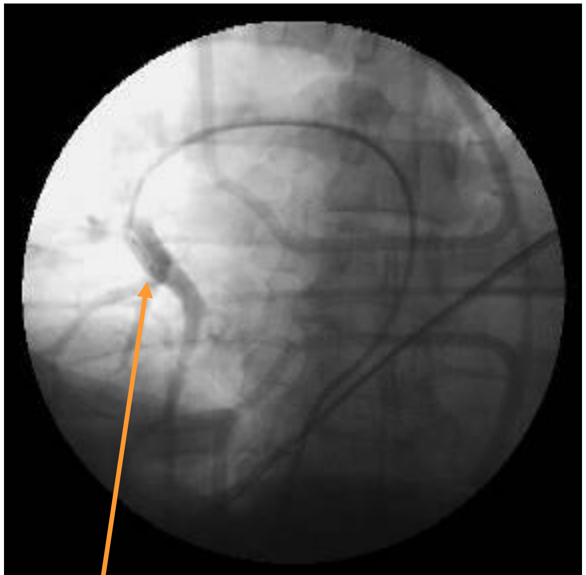
Shaft Cross Section

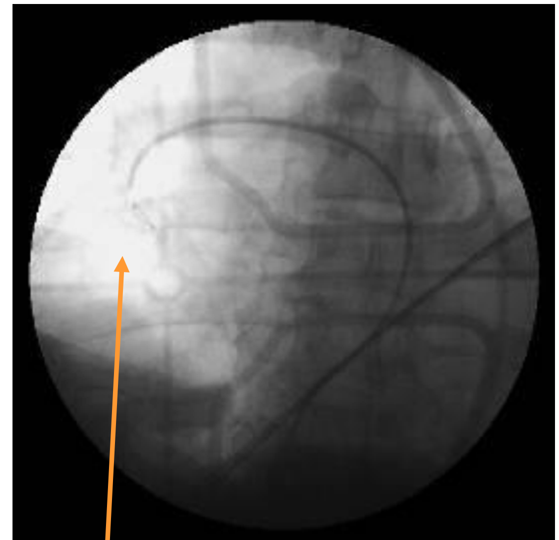


HF Delivery: Image During Implant



Sensor Does Not Impact Blood Flow





Flow around sensor

Sensor in Distal PA

Histopathology Results

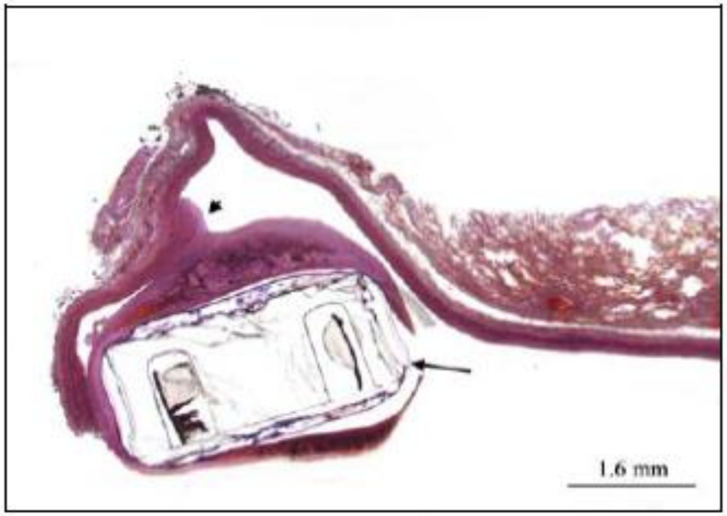


Figure 5: Device in pulmonary artery – 1.25x
Device (long arrow); Attachment to arterial wall (short arrows)

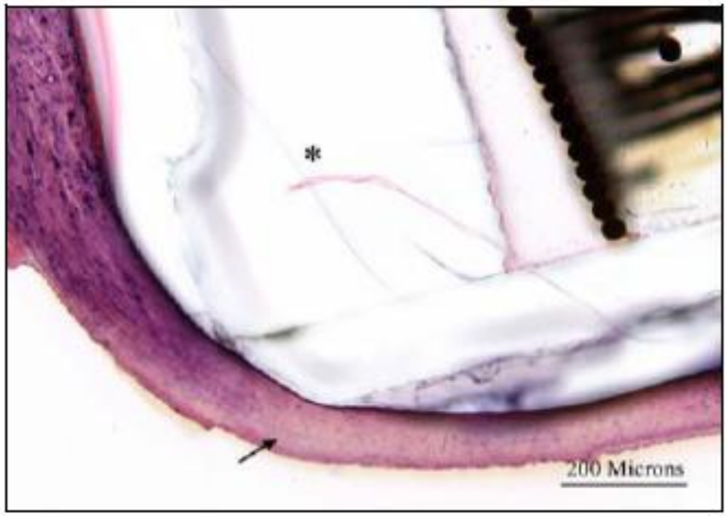


Figure 6: Device in pulmonary artery – 10x
Stable mature pseudointima (double arrow)
Wire (white arrow); Device (asterisk)

- Histopathology shows that the sensor body was covered with mature and stable fibrous pseudointima
- Sensor loops were covered with mature stable neointima
- No evidence of foreign body response or thrombosis
- Confirms positive human safety profile and histopathology results of animal studies

Ohio State University - Dr. William Abraham
Case Study Subject
52 yo White Male

CM Sensor Implant 1/30/08

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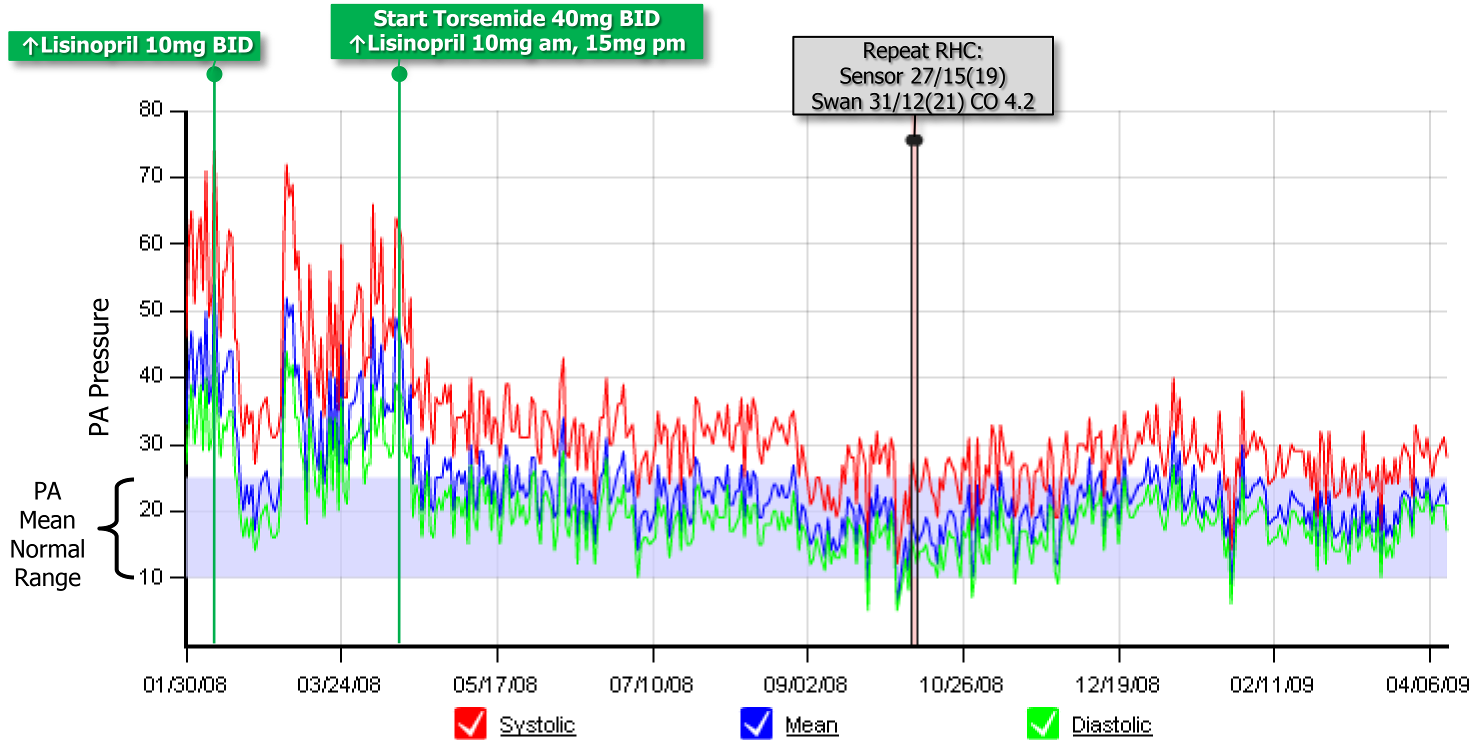


Swan at Implant:
PA 51/24(36) PCWP 16 CO 5.1 PVR 3.92

Baseline Vitals:
BP 127/75 HR 75 WGT 176 lbs. BMI 26

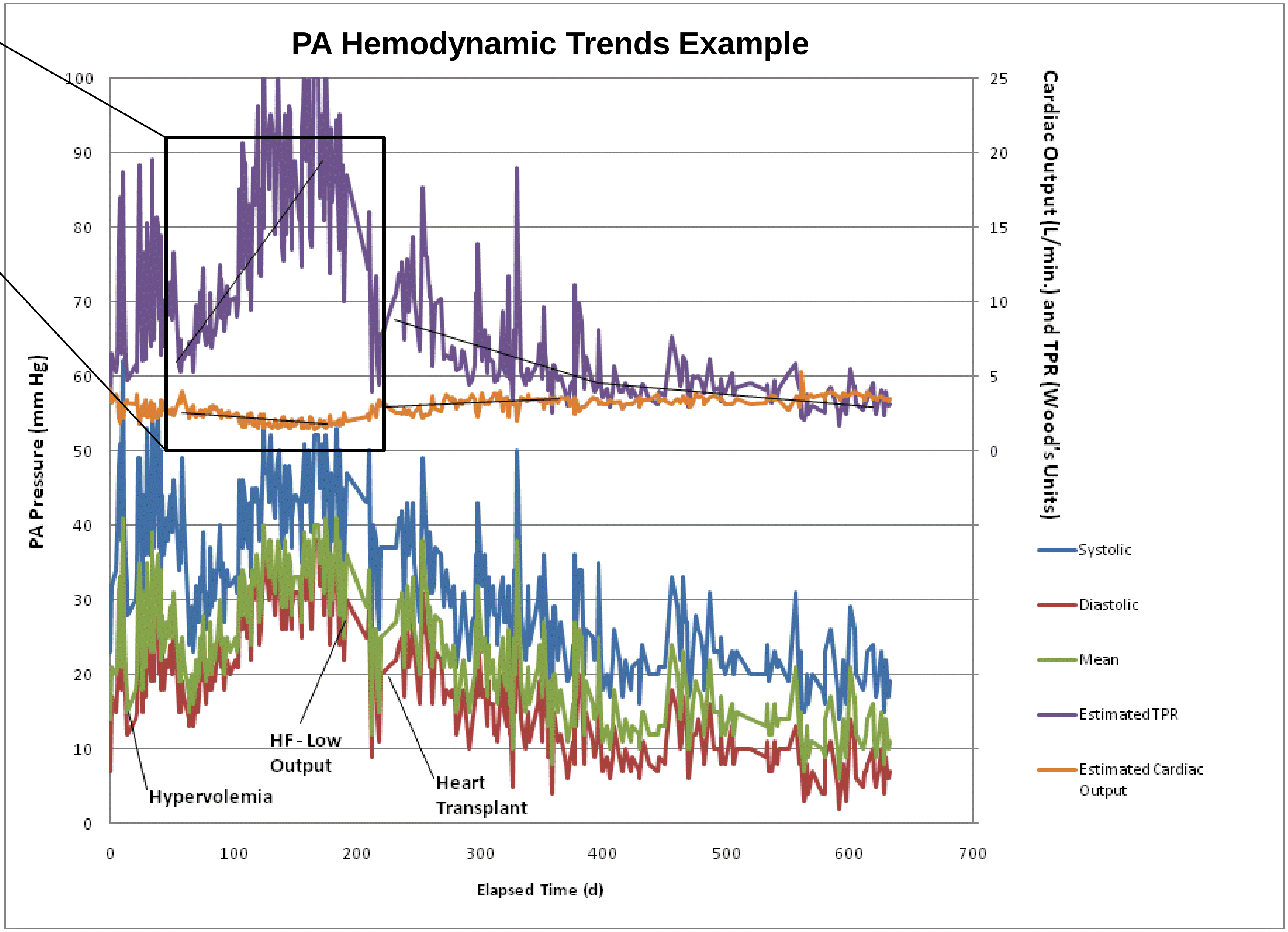
Baseline Labs:
SCr 1.2 GFR 68

Medical History
- Familial Dilated Cardiomyopathy
- ICD with CRT
- HTN
- Paroxysmal Atrial Fibrillation
- Hyperlipidemia
- Sleep Apnea
- Gout
- Depression
- Osteoarthritis
- Insomnia

Baseline Medications
Carvedilol 37.5mg BID
Lisinopril 10mg QD
Eplerenone 25mg QD
Bumetanide 1mg BID
Amiodarone 200mg BID
Digoxin 0.125mg QD
Aspirin 81mg QD
Coumadin as directed
KCL 10 meq BID

CO and TPR Estimated from Pressure Waveform

Degrading **CO** and **TPR** trends prior to Heart Transplant



Note high TPR values prior to Heart Transplant

CHAMPION US Pivotal Study Design

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Heart Failure Multi Center Randomized Controlled Study

- 75 US sites, 550 patients, NYHA Class III with 90% statistical power
- <u>Primary Endpoint</u>
  - Rate of heart failure hospitalizations within six months
- <u>Secondary Endpoints</u>
  - Percent of change in pulmonary artery pressure from baseline
  - Proportion of subjects hospitalized
  - Number of days alive outside of hospital
  - Total Quality of Life Measure from the Minnesota Heart Failure
- <u>Additional Endpoint</u> – Cost Effectiveness Substudy
- <u>Timing</u>
  - PMA filing expected in 2Q 2010, FDA Approval expected in 4Q 2010

World Wide HF Patient Enrollment: Pivotal Trial Enrollment Completed

- First Patient Implanted: December 16, 2005
- Latest Patient Implanted: October 7, 2009
- Total Patients Implanted World Wide: 602
  - South America Feasibility: 27; Germany Feasibility: 8; US Feasibility: 17
  - US Pivotal: 550 of 550
- World Wide Patient Days:
  - Total: 218,942. Mean: 365 250 days. Max: 1336 days
- Procedure Time: ~ 30 min
  - Sensor Implant: ~ 7 min
- 99% technical success with implant
- ~ 94% patient compliance
- Upcoming Presentation on Trial at ESC Meeting in Berlin on May 31, 2010

No UADEs Related to System

Conclusions

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Successful Implementation of Nanotech Attributed to:

- **Technology Development was Driven by Unmet Medical Needs**
- **Technical Needs were Uniquely Satisfied by MEMS Capabilities**
- **Design Philosophy**
- **Multidisciplinary R&D Approach**